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Clinical Findings of Infants Born to an HIV-Positive Mother: A Hospital Based Case-Control Study in Tehran, Iran

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Abstract

Background

There are contradictory results regarding association between maternal HIV infection and neonatal adverse outcomes. Therefore, in this study the neonates born from HIV-positive mothers compared with HIV-negative mothers were assessed in Tehran, Iran.

Materials and Methods

This retrospective case-control study was conducted on 50 infants born to an HIV-positive mother compared with 53 infants born to an HIV-negative mother as control group, during 8 years of a period from 2006-2015, admitted in Valiasr Hospital of Tehran. Data were gathered from medical records of patients.

Results

All children (n=53, 100%) in the case group were born through cesarean section; while 20.75% of the control group children were born by natural delivery (P=0.001). There was statistically significant difference between neonates born from HIV-positive mothers compared to HIV-negative mothers with respect to delivery method and gender (P<0.05). The mean weights (gr) were higher in the controls than the cases (3052.830±380.71 vs. 2731.80±575.90) (P=0.001). Also, a significantly increased Hemoglobin was observed in the controls (15.87±1.97 g/dL) compared to the cases (13.42±1.69 g/dL) (P=0.001). Liver functions test (LFTs) was significantly higher in case groups (P=0.005).

Conclusion

Based on the results, the mean weight and hemoglobin were lower in infants born from HIV-positive women compared with HIV-negative women. Also, LFT Disorder was higher in infants born from HIV-positive women compared with HIV-negative women.

Key Words: AIDS, Infant, HIV, Mother.

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1- INTRODUCTION

Human immunodeficiency virus (HIV) is one of the main causes of neonatal mortality and morbidity in low and middle income countries (1). Asia is the second HIV infected region in the world (2). The number of women infected with HIV in developing countries is increasing; the infection mainly affects young people with a desire to have children. Annually, about 150,000 children are infected with HIV (3). One of the most important problems around the world is transmission of HIV infection from mother to neonate (2). The use of combination antiretroviral therapy (ART) during and after pregnancy has a significant effect on reducing maternal mortality and morbidity and mother-to-child transmission of HIV, and it is safe for breast-feeding (4). The World Health Organization (WHO) recommends that programs be made to detect early HIV infection and initiate ART as soon as possible (5).

If there were not intervention programs to prevent mother-to-child transmission, the probability of HIV transmission during labor would be between 15 and 30%, and in case of breastfeeding mother, this transmission increases 20 to 45% (6). Despite substantial improvements in accessibility of Anti-Retroviral Treatment (ART), and there is no question that ART should be initiated in all pregnant women and continued thereafter (7), a significant proportion of mortality among children in sub-Saharan African countries occurs in the first 3-6 months of ART (8-10).

According the study of Khazaei et al. in 2017 the trend of HIV/AIDS mortality rate among children in Iran had a 10% increase annually from 2000 to 2015 (11). Arab et al. in 2017 showed that HIV infection was related to maternal adverse outcomes such as premature rupture of membranes (PROM), urinary tract infections (UTI), wound problems, blood transfusions, sepsis, venous thromboembolisms, postpartum infection and maternal mortality. Also, they reported that HIV infection was related to premature neonate and increase in intrauterine growth restriction (IUGR) (12). Thayaparan et al.'s study showed that 38% of the women with HIV experienced a pregnancy complication such as premature labor (9%), the total of PROM and gestational diabetes (4%), and postpartum hemorrhage (3%) (13). Some studies have showed association between maternal HIV infection and neonatal adverse outcomes, but results have been contradictory (14-16). Therefore, in this study the neonates born from HIV-positive mothers compared with HIV-negative mothers from 2006 to 2015 were assessed in Tehran, Iran.

2- MATERIALS AND METHODS

2-1. Study design and setting

This retrospective case-control study was conducted on medical records of 50 infants born to HIV-positive mothers compared with 53 infants born to HIV-negative mothers as control group, referred to infectious disease ward of Vali-e-Asr Hospital, Tehran, Iran during an 8 years period from 2006-2015. Cases and controls were matched by their mother's age (± 3 years), and parity.

2-2. Confirmation of mother's HIV status

In this study a case of HIV infection was considered as an individual with HIV infection irrespective of clinical stage confirmed by laboratory criteria according to national guideline. In Iran, a case of HIV is defined as an individual by two sequential enzyme-linked immunosorbent assay positive tests for HIV antibody followed by a positive Western blot test (17). Recommendations regarding diagnosis of HIV infection in infants and children are presented in **Appendix 1** (18).

Appendix 1: Diagnosis of HIV Infection in Infants and Children (18).

Panel's Recommendations Regarding Diagnosis of HIV Infection in Infants and Children
• Virologic assays (i.e., HIV RNA and HIV DNA nucleic acid tests [NATs]) that directly detect HIV must be used to diagnose HIV in infants and children aged <18 months with perinatal and postnatal HIV exposure; HIV antibody tests should not be used **(AII)**. • HIV RNA or HIV DNA NATs are generally equally recommended **(AII)**. • An assay that detects HIV non-B subtype viruses or Group O infections (e.g., an HIV RNA NAT or a dual-target total DNA/RNA test) is recommended for use in infants and children who were born to mothers with known or suspected non-B subtype virus or Group O infections **(AII)**. • Virologic diagnostic testing is recommended for all infants with perinatal HIV exposure at the following ages: o 14 to 21 days **(AII)** o 1 to 2 months **(AII)** o 4 to 6 months **(AII)** • For infants at higher risk of perinatal HIV transmission, additional virologic diagnostic testing is recommended at birth **(AII)** and at 2 to 4 weeks after cessation of antiretroviral prophylaxis **(BII)**. • A positive virologic test should be confirmed as soon as possible by a repeat virologic test on a second specimen **(AII)**. • Definitive exclusion of HIV infection in non-breastfed infants is based on two or more negative virologic tests, with one obtained at age ≥1 month and one at age ≥4 months, or two negative HIV antibody tests from separate specimens obtained at age ≥6 months **(AII)**. • Some experts confirm the absence of HIV at 12 to 18 months of age in children with prior negative virologic tests by performing an HIV antibody test to document loss of maternal HIV antibodies **(BIII)**. • Since children aged 18 to 24 months with perinatal HIV exposure occasionally have residual maternal HIV antibodies, definitive exclusion or confirmation of HIV infection in children in this age group who are HIV antibody-positive should be based on an HIV NAT **(AII)**. • Diagnostic testing in children with nonperinatal exposure only or children with perinatal exposure aged >24 months relies primarily on the use of HIV antibody (or antigen/antibody) tests; when acute HIV infection is suspected, additional testing with an HIV NAT may be necessary to diagnose HIV **(AII).**
Rating of Recommendations*:* A=Strong; B=Moderate; C=Optional **Rating of Evidence*:*** I = One or more randomized trials in children† with clinical outcomes and/or validated endpoints; I* = One or more randomized trials in adults with clinical outcomes and/or validated laboratory endpoints with accompanying data in children† from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; II = One or more well-designed, nonrandomized trials or observational cohort studies in children† with long-term outcomes; II* = One or more well-designed, nonrandomized trials or observational studies in adults with long-term clinical outcomes with accompanying data in children† from one or more similar nonrandomized trials or cohort studies with clinical outcome data; III = Expert opinion.

2-3. Eligibility criteria

In this study all known HIV-infected women who gave birth in Vali-asr hospital during 2006-2015 were retrospectively reviewed. Cases with incomplete records were excluded from the study.

2-4. Measurement tool

We abstracted data from medical records of patients and required information including: gender, delivery method, economic status, icterus, hepatosplenomegaly, arterial blood gas (ABG) disorders, liver enzyme disorders, intrauterine growth restriction (IUGR), birth weight, hemoglobin, height, head circumference, gestational age, and Apgar

regarding hospital records of investigated infants were gathered. Investigation of the medical records was conducted by the pediatric residents.

2-5. Data analysis

Qualitative data were presented with frequency and percentage and quantitative variables were presented with mean ± standard deviation (SD). Normality of data was assessed with Kolmogorov–Smirnov test (in this study normality assumption was held for investigated variables). The association of mother's HIV status with clinical characteristics of the infant was examined by using the Chi- square and exact Fisher's test. The mean comparisons of investigated variables between groups were assessed through student t. test. All the analyses were done using SPSS software (version 23.0) (SPSS Inc., Illinois, USA). P-value less than 0.05 was considered as significant.

2-6. Ethics

Ethical approval for the study was obtained from the Institutional Review Board of Tehran University of Medical Sciences according to Helsinki Declaration. The name and personal information of the patients remained confidential.

3- RESULTS

A total of 103 infants were included in the study. The study participants (50 cases and 53 controls) were compared on the basis of their baseline and clinical characteristics. Baseline characteristics of infants in case and control groups are shown in **Table.1**. As shown, there was statistically significant difference among them with respect to delivery method (the rate of cesarean was 100% in cases compared to 79.25% in controls [P=0.001]), and gender (P=0.022).

Table-1: Baseline characteristics of infants in neonates born from HIV+ mothers compared with HIV- mothers.

Variables		Born from HIV+ mothers (n=50)	Born from HIV- mothers (n=53)	P-value
Gender	Boy	23 (46.00)	13 (24.53)	0.022
	Girl	27 (54.00)	40 (75.47)	
Delivery Method	NVD	0	11(20.75)	0.001
	C/S	50 (100.00)	42 (79.25)	
Economic Status	Medium	44 (88.00)	48 (90.57)	0.67
	Low	6 (12.00)	5 (9.43)	

NVD: Normal vaginal delivery, C/S: Cesarean section.

Clinical characteristics of infants in the case and control group are compared in **Table.2**. Only three infants in case group were IUGR and all of them were negative for hepatosplenomegaly. There was no statistically significant difference between two groups with regards to icterus (9=0.4). In contrast to the control group that had no cases of liver functions test (LFT), and ABG Disorder, these disorders had occurred in 7 and 3 patients in the case group, respectively.

Table-2: Comparison of clinical characteristics of infants in neonates born from HIV^+ mothers compared with HIV^- mothers.

Variables		Born from HIV+ mothers (n=50)	Born from HIV- mothers (n=53)	P-value
IUGR	Positive	3 (6.00)	0	0.11
	Negative	47 (94.00)	53 (100.00)	
Icterus	Positive	17 (34.00)	14 (26.42)	0.40
	Negative	33 (66.00)	39 (73.58)	
Hepatosplenomegaly	Positive	0	0	-
	Negative	50 (100.00)	53 (100.00)	
LFT Disorder	Positive	7 (14.00)	0	0.005
	Negative	43 (86.00)	53 (100.00)	
ABG Disorder	Positive	3 (6.00)	0	0.11
	Negative	47 (94.00)	53 (100.00)	

IUGR: intrauterine growth restriction; LFT: liver function test; ABG: arterial blood gas.

The mean weight (gr) was higher in the controls than the cases (3052.830±380.71 vs. 2731.80±575.90) (P=0.001). Also, a significantly increased Hemoglobin was observed in the controls (15.87±1.97 g/dL) compared to the cases (13.42±1.69 g/dL) (P=0.001) (**Table.3** and **Figure.1**). But there was not a statistically significant difference between two groups with regards to height, head circumference, gestational age and Apgar (**Table.3**).

Table-3: Anthropometrics and hematological parameters in neonates born from HIV^+ mothers compared with HIV^- mothers.

Variables	Born from HIV+ mothers (n=50)	Born from HIV- mothers (n=53)	P-value
Weight (gr)	2731.80±575.90	3052.830±380.71	0.001
Height (cm)	47.10±5.99	45.45±9.95	0.31
Head circumference (cm)	35.10±3.31	36.38±6.52	0.22
Gestational Age (week)	37.26±1.47	37.70±1.49	0.13
Apgar	8.92±0.40	9.00±0.00	0.15
Hemoglobin (g/dL)	13.42±1.69	15.87±1.97	0.001

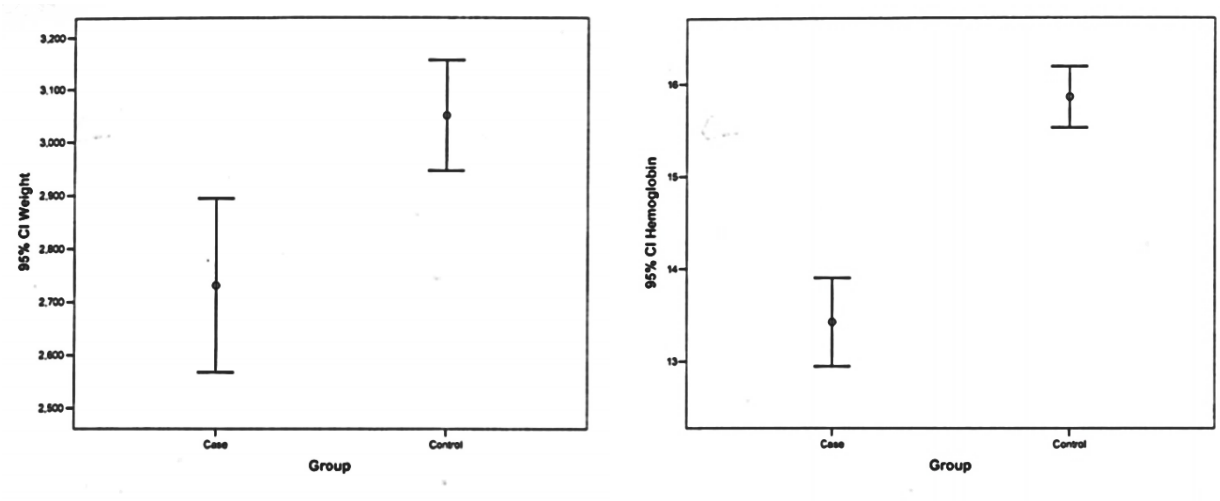

Fig.1: Comparison of weight and hemoglobin in neonates born from HIV+ mothers compared with HIV- mothers.

4- DISCUSSION

This study was conducted to compare clinical findings of the neonates born from HIV-positive mothers with neonates born from HIV-negative mothers. Our findings reported that the mean weight and hemoglobin were lower in infants born from HIV-positive women compared with HIV-negative women. Also, LFT disorder was higher in infants born from HIV-positive women compared with HIV-negative women, but there was not a statistically significant difference between two groups as regards height, head circumference, gestational age and Apgar. A study by Feleke et al. in Addis Ababa was performed and they reported that the odds of anemia was 2.54 times higher for infants born from HIV-positive mothers compared with those born from HIV negative mothers (19). This finding was in line with our study and the study from Indonesia (20). This is due to decrease of hemoglobin level in mothers with positive-HIV and this decreasing in the iron transferred to infant (20). Ickovics et al. in 2000 showed that women with HIV seropositive were 2.6 times more likely to have an infant of low birth weight (LBW) (21). Ahmed et al. in their meta-analysis showed that maternal HIV infection in women who have not received antiretroviral therapy is associated with preterm birth, low birth weight, small for gestational age, and stillbirth (8). In our study, the mean weight (gr) was lower in the case group than the control group. Silverman et al. reported that increased liver function, especially aspartate aminotransferase (AST) concentrations in 58% of the newborns were evaluated, but they did not shown symptoms of Icterus (22). This is in line with present study. However, El Beitune et al.'s study in 2007 reported that there was not a significant association between the use of antiretroviral drugs during pregnancy and adverse outcomes on neonatal amylase and hepatic parameters in neonate (23). In our study, there was significant association between cesarean section and HIV-positive women compared with HIV-negative women. Arab et al. showed that HIV-positive women were also more likely to have a cesarean delivery. They reported that 60% of HIV-positive women delivered by cesarean section compared with 31% of HIV-negative women (12). The findings of Kourtis et al. approved our results (24). However, highly active anti-

retroviral therapy (HAART) was reported that has been very effective in prevention of mother-to-child transmission, therefore elective cesarean section was not recommended (25).

4-1. Study Limitations

Our study had some limitations: (a) There was a little information about patients treatment for HIV, especially the duration and treatment time. (b) Low sample size was the other limitation of the present study. However, despite these limitations, our findings showed that pregnancy in HIV-infected women was associated with some newborn complications. Therefore, pregnant women who are HIV-positive should be followed in health centers as highrisk groups.

5- CONCLUSION

Our findings showed that the mean weight and hemoglobin were lower in infants born from HIV-positive women compared with HIV-negative women. Also, LFT Disorder was higher in infants born from HIV-positive women compared with HIV-negative women. Therefore, pregnant women with HIV-positive should be followed in health centers as high risk groups.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGEMENTS

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